

REMARKS

The Official Action of 8 May 2006 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claim 115 has been amended with the incorporation of the recitations formerly in claims 116 and 117, and the latter claims have been canceled. Claim 115 has also been amended in a manner which more clearly avoids the rejection under 35 USC 112, first paragraph, appearing on pages 4-6 of the Official Action, as discussed below.

New claims 122-135 have been added more completely to define the subject matter which Applicants regard as their invention. Support for the recitations in these claims appear, for example, in original claims 115 and 118-121, and in the specification at paragraph [0034] on page 9 and paragraphs [0064] and [0065] on page 22.

The amendment to claim 115 is respectfully believed to remove the basis for the double patenting rejection appearing at pages 3-4 of the Official Action. In this connection, Applicants respectfully note that the rejection was not applied against the subject matter of claims 116 and 117, which subject matter has now been incorporated into claim 115.

Claims 115-117 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The rejection is based upon the Examiner's contention that the claims read on treating all types of tumors and cancers, while the present specification allegedly does not contain sufficient guidance as to how the claimed invention will treat all types of tumors and cancers. Applicants respectfully submit that this rejection is at least inconsistent with the prior art rejection based on Cash, Jr. et al as primary reference, wherein the reference is alleged to teach the treatment of (all) tumors by radiosurgery with (all) contrast agents comprising (all) heavy elements, such as iodine (see, Cash, Jr. et al at, for example, claim 1). Although, as discussed below, Cash, Jr. does not show or suggest the claimed method for selective disruption of cells using rose bengal, it does show a method for radiosurgery that the Examiner contends represents the state of the art. Assuming for the sake of argument that this were true, Applicants respectfully remind the Examiner that, in assessing the enablement of the present specification, the Examiner must take into account the presumptively valid teachings of the Cash, Jr. patent as to the state of the art, the relative skill of those in the art, and the predictability of the art of treating tumors by radiosurgery.. See Wands factors 6-8 as identified on page 5 of the Official Action.

In any event, the claims have now been amended such that the claimed method is no longer directed to a method for treating tumors and cancers generally, but to a method for the selective disruption of cells in a selected region of a subject. Specifically, the breadth of the claim has been made to track the disclosure in the specification in paragraphs [0062] to [0065], which describes the accumulation of rose bengal in lysosomes of cells and the disruption of the cells that results as a consequence of shining line emission x-rays upon the cells in which rose

bengal has accumulated. Applicants respectfully submit that the Examiner has no basis on which to cast doubt on the enablement of this presumptively accurate disclosure. See MPEP 2164.04 (“A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.”)

In line with the above, Applicants respectfully submit that the rejection under 35 USC 112, first paragraph, has been overcome. Applicants respectfully request withdrawal of the rejection.

Claims 115-117 stand rejected under 35 USC 103(a) as allegedly being unpatentable over Cash, Jr. et al in view of Wang and Ariel et al. Applicants respectfully traverse this rejection.

The claimed invention is based on Applicants’ realization that rose bengal, which is a food dye that has not heretofore been known to be toxic in human cells, can be used as a chemotherapeutic agent by administering the same so that it accumulates in the lysosomes of cells and subsequently irradiating the cells with line emission x-rays that lead to a massive Auger cascade and disruption of the lysosomes and cell death. This is described in the specification at

paragraph [0063] on page 22.

In contrast, the art cited by the Examiner does not show or suggest the use of rose bengal as a chemotherapeutic agent, either alone or in combination with radiosurgery. The primary reference, Cash, Jr. et al, describes the use of contrast agents **that are known to have damaging effects on cells** for enhancing radiotherapy or radiosurgery. See Cash, Jr. at column 2, lines 33-50. There is nothing in the reference that would show or suggest, with even a reasonable expectation of success, that a food dye that is not known as a chemotherapeutic agent would be effective in selectively disrupting the cells that are irradiated with line emission x-rays according to the claimed method.

There is *a fortiori* nothing in the reference that would show or suggest, with even a reasonable expectation of success, that rose bengal would be effective if administered orally, enterically or intravenously (see claims 127-129). To the contrary, Cash, Jr. et al teach away from this. See, Cash, Jr. at column 7, lines 53-56 (“We have found that intravenous injection can achieve interesting levels of dose enhancement, but usually not a large enough differentiation between tumor and normal tissue to kill the tumor with a single dose without harming surrounding tissue.”).

Cash, Jr. et al also teach away from the method defined in claims 125 and 126, which require that the irradiating be performed at least 12 hours after administration of the rose bengal (see specification at paragraph [0065] on page 22). In contrast, Cash, Jr. et al teach that the

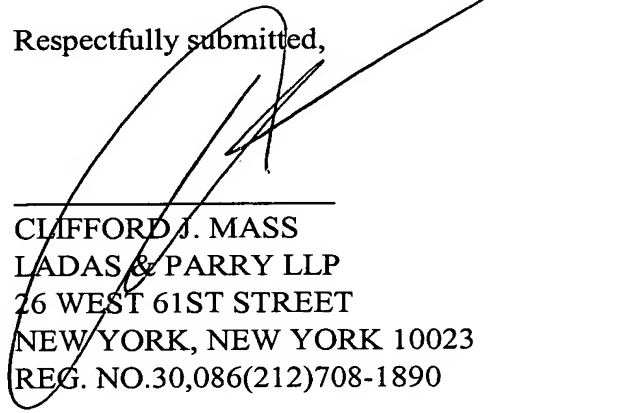
irradiating should be done within at most several hours. See, Cash, Jr. at column 7, lines 44-52 (“Therefore, the contrast agent is present for only a relatively brief period. The therapy of the present invention should be performed within a half-hour after injection of the iodine if it is to be fully effective. A contrast agent that would remain in high concentration for a period of several hours is preferred.”).

The Examiner considers that one of the secondary references, Ariel et al, teaches rose bengal as a well-known anticancer used to treat cancer of the liver, but Applicants respectfully disagree. Ariel et al teach that rose bengal is useful in hepatic gammascanning as an aid in the selection of patients for cancer therapy (see Ariel et al at page 800, first full paragraph). This is in accord with the use of rose bengal described in paragraph [0063] at page 22 of the present specification. It is also in accord with the definition of rose bengal, as shown in the attached dictionary definition (“A bluish-red dye used as a stain for bacteria, as a stain in the diagnosis of keratitis sicca, and **in tests of liver function.**” Emphasis added.). The use of this compound for the selective disruption of cells in combination with line emission x-rays of selected energy was not known prior to the disclosure in the present specification.

In view of the above, Applicants respectfully submit that the cited references are incompetent to set forth even a *prima facie* case of obviousness for the invention as presently claimed. Accordingly, Applicants respectfully request withdrawal of the prior art rejection of record.

Applicants respectfully submit that all rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,



CLIFFORD J. MASS
LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NEW YORK 10023
REG. NO.30,086(212)708-1890